

Treating hot flushes without hormone replacement therapy

Many women who are either unwilling or unable to take hormone replacement therapy seek plant-based remedies to alleviate vasomotor symptoms that accompany the menopausal transition. Here, the author outlines the primary alternative therapies used to combat hot flushes.

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Roughly 4,000 women in the United States turn 50 daily, joining the ranks of the 40 million American women currently menopausal. A survey published by the North American Menopause Society in 1998 found that the most common reason that women in

this age group visit their physicians is to seek relief from everyday menopausal symptoms such as hot flushes. While temporary, hot flushes can last up to 2 years and are a result of changes in estrogen levels.

Despite HRT's proven efficacy in treating this plaguing symptom, many patients are fearful that HRT might lead to an increased risk of breast or uterine cancer or that it may cause unpleasant side effects such as mood swings, depression, or continued menstrual periods.¹ One study of 2,500 postmenopausal women found

that 20% to 30% never fill their initial HRT prescriptions, 10% of those who use estrogen do so only intermittently, and an additional 20% discontinue their therapy within 8 months.² Furthermore, HRT is contraindicated

in about 10% of postmenopausal women.³

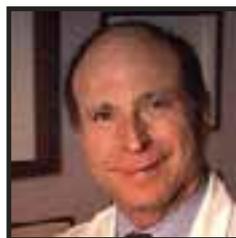
With such an enormous number of women either unwilling or unable to take HRT, it is important to consider what alternatives an Ob/Gyn can offer for treating vasomotor symptoms. These choices certainly aren't new. If we look back to the 1899 Merck Manual, recommendations included ammonia, camphor, *Cannabis indica*, opium, and suc ovarian (the "juice" from cow ovaries crushed at the slaughterhouse). While these therapeutic agents have fallen by the wayside, a number of alternative treatments for hot flushes are in use today by an increasing number of menopausal women.

How pervasive are alternative therapies?

So-called alternative approaches to menopause are used so widely that it might be more accurate to consider HRT as the true alternative medicine. Statistics presented at the National Institutes of Health on October 27, 2000, indicate that nearly half of all menopausal women are using complementary therapies, including vitamins, herbs, and soy products, to help treat their symptoms. Twenty-one percent of the women surveyed used complementary or alternative therapies alone, and 25% said they used both conventional and alternative methods. Taken together, that is more than twice the 19% who said they used conventional HRT only. Given this enormous usage, it should come as no surprise that, in 2001, the dietary supplement industry likely exceeded \$12 billion in sales in the United States alone.⁴ For many women, the decision to use an alternative is

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**Women in
Western countries
have an
80% incidence
of hot flushes.**

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not so much dissatisfaction with conventional treatment, but that they regard the complementary agents as more congruent with their own values, beliefs, and philosophical orientations toward health and life.⁵ This article will review some of the more commonly used alternatives that women use for the treatment of hot flashes. Patients should take an alternative for at least 1 month before initiating another one, to determine if it is achieving the desired effect.

Soy

Much of the excitement about the health benefits of soy, a staple of the Asian diet for 5,000 years, stems from epidemiological studies. The Asian diet, which is rich in isoflavones, is associated with a reduced risk of breast cancer, heart disease, and osteoporosis. Asian women also report fewer hot flashes than do their Western counterparts.⁶ One study showed that women in Western countries have an 80% incidence of hot flashes, while Asian women living in China have an incidence of only 20%.⁷ Clearly, factors other than soy also must be considered before we can make a direct cause-and-effect correlation. To that end, many studies have been conducted on the health benefits of soybeans, a rich source of the isoflavones genistein and daidzein.

Isoflavones are phytoestrogens with a heterocyclic phenol structure that is similar to estrogen. Their potency is between 1×10^4

and 1×10^5 the activity of 17β -estradiol.⁸ Although their potency is low, their serum concentrations can reach levels several orders of magnitude higher than those of physiologic estrogens. It is generally believed that isoflavones act as a selective estrogen receptor modulator (SERMs), exerting anti-estrogenic effects in the high-estrogen environment of premenopause and estrogenic effects in the low-estrogen environment of postmenopause.

An increasing number of studies suggest that soy and soy isoflavones—in the form of soy flour, soy protein, and dietary supplements—may play an important role in the treatment of hot flashes (*Table 1*). In general, the average amount of isoflavones consumed in a typical Asian diet is approximately 50 mg. (One gram of soy protein contains approximately 1 mg of isoflavones.) As shown in the table below, all of the methods of taking soy decrease the number and/or severity of hot flashes.

All of the soy studies also confirm the existence of a placebo effect on the treatment of hot flashes. Even so, the soy group typically reports a 15% to 20% greater reduction in symptoms than does the placebo group. This difference between the soy and control groups has led skeptics to believe that the differences may be statistically significant but clinically insignificant. I believe that thinking is wrong. Women who have hot flashes tend to have lower sleep efficiencies and longer

Data suggest that soy is safe and effective in dosages of 40 g of soy protein or 50 mg of soy isoflavones per day.

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The role of soy in the treatment of hot flashes				
STUDY	NO. PATIENTS	DESIGN	↓ FLUSHES SOY (%)	↓ FLUSHES CONTROL (%)
Murkies 1995	58	45 g soy flour	40	25
Brzezinski 1997	73/72	Mostly soy 1/4 diet, some flaxseed	54	35
Albertazzi 1998	51/53	60 g soy protein	45	30
Scambia 2000	20/19	50 mg/d isoflavones	45	25
Upmalis 2000	177	50 mg/d isoflavones	30	20

SOURCE: Seibel MM. *The Soy Solution for Menopause: An Alternative to Estrogen*. New York, NY: Fireside Press; 2002.

TABLE 1

Adverse effects

TABLE 2

SOY	<ul style="list-style-type: none"> ■ Bloating, flatulence
BLACK COHOSH	<ul style="list-style-type: none"> ■ Abdominal pain, nausea, headaches, dizziness, trembling limbs
DONG QUAI	<ul style="list-style-type: none"> ■ Photodermatitis, rash
EVENING PRIMROSE OIL	<ul style="list-style-type: none"> ■ Nausea, softening of stools, headaches, seizures
RED CLOVER	<ul style="list-style-type: none"> ■ Blood thinning
HRT	<ul style="list-style-type: none"> ■ Depression, headaches or migraines, breast tenderness, hair loss, nausea or vomiting, vaginal bleeding, jaundice, candidiasis, weight gain, loss of libido, blood clots, increased risk of gall bladder disease and uterine and breast cancer

REM latencies than women who do not experience this vasomotor symptom.¹⁴ By lowering the frequency of hot flushes by 40% or more, patients who take soy will have 40% or more greater sleep efficiencies. That may improve their quality of life sufficiently to make HRT unnecessary.

Soy has been safely consumed by hun-

dreds of millions of people without complications, with the possible exception of soy allergies (*Table 2, 3, and 4*). The literature suggests it is safe and effective in dosages of either 40 g of soy protein or 50 mg of soy isoflavones per day. Soy does not stimulate the uterine lining and may be protective of the endometrium if taken with estrogen. The incidence of breast cancer is one-fourth as high in Asia as it is in the United States; many studies have shown soy to be protective of breast tissue. However, soy may stimulate breast tissue in women with a history of breast cancer.

Black cohosh

A member of the buttercup family, black cohosh has a long history in folk medicine, especially among Native Americans who boiled the root in water and drank the resulting beverage to treat dysmenorrhea, labor pain, upset stomach, and arthritis. In Germany, extracts of black cohosh have been used since the 1940s.

Many substances have been identified in the rhizome, but it is uncertain what the majority of them do or, in fact, which are active ingredients.¹⁵ The effectiveness of black cohosh is based on the total amount of triterpenoid glycosides, typically standardized to 2.5%.¹⁶

Several studies, most of them in the German literature, have shown that black cohosh yields a significant improvement in hot flushes, with reductions of up to 80% reported.¹⁷⁻¹⁹ The usual dosage is 40 drops of the extract twice daily for 6 to 8 weeks, or one to two 20-mg tablets twice daily with liquid (not to be chewed or sucked).

Side effects are uncommon, but occasional stomach pains and intestinal discomfort, dizziness, nausea, severe headaches, stiffness, and trembling limbs have been noted. Germany's Commission E, which is similar to the U.S. Food and Drug Administration (FDA), recommends that black cohosh not be used for more than 6 months

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Drug interactions

TABLE 3

SOY	<ul style="list-style-type: none"> ■ Thyroid hormones
BLACK COHOSH	<ul style="list-style-type: none"> ■ Iron therapy medications
DONG QUAI	<ul style="list-style-type: none"> ■ Treatment with anticoagulants such as warfarin
EVENING PRIMROSE OIL	<ul style="list-style-type: none"> ■ Anticonvulsants and tricyclic antidepressants
RED CLOVER	<ul style="list-style-type: none"> ■ Anticoagulants such as warfarin, heparin, clopidogrel, pentoxifylline, or aspirin
HRT	<ul style="list-style-type: none"> ■ Antibiotics

Contraindications

TABLE 4

SOY
■ Patients with hypothyroidism. (Soy may bind thyroid medication, thus lowering absorption, but if taken at other times or in supplement form, it should not have an effect on thyroid function.)
BLACK COHOSH
■ Patients with iron deficiencies
DONG QUAI
■ Patients with coagulopathies or very heavy menstruation and acute viral infections such as colds or influenza
EVENING PRIMROSE OIL
■ Patients with temporal lobe epilepsy or schizophrenia
RED CLOVER
■ Patients with coagulopathies
HRT
■ Women who have had breast or uterine cancer, unusual vaginal bleeding, or severe liver disease

since no studies have been conducted for longer periods of time. Although most data on the safety of black cohosh with regard to breast tissue are reassuring, use caution when administering it to a patient with a history of breast cancer, as black cohosh is a weak estrogen (Table 2, 3, and 4).

Dong quai (*Angelica sinensis*)

Dong quai, a common Chinese herb extracted from the *Angelica sinensis* root, has become popular in the U.S. In contrast to China, where it is sold as part of a mixture that includes several other herbs, dong quai typically is sold in the U.S. as a single herb.

Although some women report improvements in their vasomotor symptoms, there have been very few studies on the effects of dong quai on menopause. In one study of 71 postmenopausal women over a 24-week period, researchers could not demonstrate a difference between dong quai and placebo in alleviating vasomotor symptoms.²⁰ The investigators suggested that studying the effects of dong quai alone, rather than in

combination with other herbs, may have been a factor in their findings.

Two caveats: Dong quai increases photosensitivity, so women taking the herb should be cautioned that too much exposure to sunlight may result in a rash. Also, it has been reported to potentiate the effects of warfarin (Table 2, 3, and 4). It should not be used during pregnancy.²¹

Evening primrose (*Oenothera biennis*)

Native Americans consumed the leaves, roots, and seedpods of this plant for food, and made extracts from it to treat a variety of conditions. Today, the flowers and seeds are pressed to make oil that is high in gamma-linolenic acid (GLA) and essential polyunsaturated fatty acids, which convert into prostaglandins. Evening primrose oil also is a good source of linoleic acid and the omega-6 fatty acid γ -linoleic acid.

Although there are a number of good studies in which evening primrose oil has been used to successfully treat eczema and several other conditions with few side effects, it appears to have no benefit over placebo for hot flushes.²²

Patients should be warned that mild upset stomach, indigestion, nausea, softening of stools, and mild headaches may occasionally occur. Also, evening primrose is contraindicated in women taking conventional medication for temporal lobe epilepsy or schizophrenia, as the substance decreases the efficacy of those drugs (Table 2, 3, and 4).

Red clover (*Trifolium pratense*)

Red clover is a plant that contains the phytoestrogens formononetin, biochanin A, daidzein, and genistein. It was originally used by Native Americans to treat whooping cough, gout, and cancer.

Two clinical trials conducted in Australia failed to demonstrate that red clover extract was more effective than placebo in reducing vasomotor symptoms.^{23,24} However, one

Because red clover contains warfarin, high dosages may cause the blood to thin.

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study found that women who took 40 mg of red clover per day—the recommended dosage—experienced a significant reduction in hot flashes.²⁵

There is still little information on whether red clover will have any effect on the uterine lining or breast tissue. Because red clover contains warfarin, high dosages may cause the blood to thin (Table 2, 3, and 4).

Conclusion

Whether to take HRT is one of the major decisions women in perimenopause or early menopause have to make. The overwhelming majority will decide against it, either out of fear of potential risks or simply to avoid unpleasant side effects. In fact, several studies have shown that only 15% to 20% of women will take HRT for more than a year.² Even women who do agree to take HRT frequently demonstrate poor compliance.

But patients who decline HRT do need—and will have—other choices to help them weather vasomotor symptoms that can greatly disrupt their lives. Many women find these plant-based alternatives an important option that allows them to control their hot flashes without taking HRT.

As clinicians start to recommend alternative supplements to their menopausal patients, they should do so with an understanding of the expected results, potential risks and benefits, and how the recommendation may interact with other medications. If these guidelines are followed, physicians may recommend alternative treatments with the same confidence they have in prescription drugs. ■

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Key points

- About 21% of women surveyed use complementary or alternative therapies alone, and 25% said they used both conventional and alternative methods.
- Women who take 50 mg of soy isoflavones daily typically report a 40% to 50% reduction in hot flashes.
- Black cohosh yields up to an 80% improvement in hot flashes.
- Doses of 40 mg of red clover per day effect a significant reduction in hot flashes.

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